In the United States Court of Federal Claims
OFFICE OF SPECIAL MASTERS

BERLIN V. BRAVO,	*	
	*	No. 17-501V
Petitioner,	*	Special Master Christian J. Moran
	*	
v.	*	
	*	Filed: May 31, 2023
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
	*	
Respondent.	*	

Sol P. Ajalat, Ajalat & Ajalat, LLP, North Hollywood, CA, for petitioner;
Colleen Hartley, United States Dep't of Justice, Washington, DC, for respondent.

PUBLISHED DECISION DENYING ENTITLEMENT[1]

Berlin Bravo is claiming that a human papilloma virus ("HPV") vaccine either caused her to suffer multiple sclerosis or caused her previously undiagnosed multiple sclerosis to worsen. The Secretary disputes both claims. Ms. Bravo has filed a series of reports from experts, of which some do not meaningfully advance her claims. In contrast, the Secretary has also presented multiple reports from experts, and these are more persuasive. Similarly, the parties have advocated through memoranda. Ms. Bravo's briefs are not effective, and the Secretary's brief is convincing. The primary flaw with Ms. Bravo's evidence is that she has not

[1] Because this Decision contains a reasoned explanation for the action taken in this case, it must be made publicly accessible and will be posted on the United States Court of Federal Claims' website, and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc, in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). This means the Decision will be available to anyone with access to the internet. In accordance with Vaccine Rule 18(b), the parties have 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. Any changes will appear in the document posted in the website.

persuasively shown how an HPV vaccination can cause pre-existing multiple sclerosis to worsen. An independent and second problem is that Ms. Bravo has not presented a logical sequence of cause and effect showing that the HPV vaccination harmed her. Accordingly, Ms. Bravo is not entitled to compensation.

Due to the issues raised, the decision is organized unusually. The standards for adjudication are set forth at the beginning. The next section (Section II) describes the people whom Ms. Bravo and the Secretary have retained. Section III starts the analysis by explaining the basis for a finding that Ms. Bravo likely suffered from multiple sclerosis before she received the third dose of the HPV vaccine. Section III includes a summary of the procedural history relevant to determining when Ms. Bravo began to have multiple sclerosis as well as a summary of the medical records through her initial hospitalization for multiple sclerosis.[2] The analysis continues in Section IV, which resolves whether Ms. Bravo has presented preponderant proof that the HPV vaccination significantly aggravated her condition. Within Section IV, parts are devoted to Ms. Bravo's more recent medical history, the procedural history regarding a claim that the HPV vaccination harmed her, and the elements of significant aggravation. The evaluations in Section III and Section IV are the foundation for a determination that a hearing is not needed (Section V). Finally, the decision ends with additional comments (Section VI) and a conclusion (Section VII).

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[2] The procedural history regarding the gathering of medical records does not affect the outcome of the case. Therefore, those events are not set forth in this Decision.

Likewise, as Ms. Bravo's motion for the undersigned's recusal is irrelevant to the outcome of her claim, it does not factor into the analysis section of this Decision. However, a summary is provided here.

Ms. Bravo argued that the undersigned was biased against her and/or her attorney based on (1) a rescinded March 2, 2020 order requiring Ms. Bravo's attorney to associate with an attorney more experienced in the Vaccine Program to assist Ms. Bravo in developing a significant aggravation claim, and (2) an April 9, 2020 order requiring Ms. Bravo to submit an affidavit, witnessed by a notary public, in which she affirmed her retention of her attorney as her counsel of record. Pet'r's Mot., filed Apr, 27, 2020. The undersigned denied the motion, as it did not raise any legitimate bases for recusal. All assessments were developed during the course of the litigation. Order Denying Motion for Recusal, issued May 27, 2020.

On June 12, 2020, Ms. Bravo filed a motion to review the order denying recusal. As the order was not a final "decision" as defined by the Vaccine Program, Ms. Bravo's motion was denied for lack of jurisdiction. Bravo v. Sec'y of Health & Hum. Servs., 149 Fed. Cl. 333, 335 (2020).

I. Standards for Adjudication

A petitioner is required to establish her case by a preponderance of the evidence. 42 U.S.C. § 300aa–13(1)(a). The preponderance of the evidence standard requires a "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010) (citations omitted). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Human Servs., 931 F.2d 867, 873 (Fed. Cir. 1991).

Distinguishing between "preponderant evidence" and "medical certainty" is important because a special master should not impose an evidentiary burden that is too high. Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1379-80 (Fed. Cir. 2009) (reversing special master's decision that petitioners were not entitled to compensation); see also Lampe v. Sec'y of Health & Human Servs., 219 F.3d 1357 (Fed. Cir. 2000); Hodges v. Sec'y of Health & Human Servs., 9 F.3d 958, 961 (Fed. Cir. 1993) (disagreeing with dissenting judge's contention that the special master confused preponderance of the evidence with medical certainty).

II. People Retained in this Litigation

Ms. Bravo retained a total of five people. The most credible person was a neuroradiologist, David Wilson. Ms. Bravo also retained two people who have often expressed opinions that vaccines harmed someone, Lawrence Steinman (a neurologist with additional qualifications in immunology) and Yehuda Shoenfeld (an immunologist). Ms. Bravo also submitted reports from two people who have participated in the Vaccine Program much less frequently, Sin Hang Lee (a pathologist) and Christopher Shaw, who has earned a Ph.D. and researches neuroplasticity and neuropathology.

The Secretary has presented reports from three people. Like Ms. Bravo, the Secretary retained an expert to discuss neuroradiologic studies, Jonathan Kleefield. Otherwise, to address the claims that the HPV vaccination harmed Ms. Bravo, the Secretary relied upon two people whom he has often retained. The first is Subramaniam Sriram, a neurologist with additional qualifications in immunology. The second is Neil Romberg, an immunologist.

Collectively, the opinions from these people helped understand the issues, namely, when Ms. Bravo began to suffer from multiple sclerosis and whether the HPV vaccination contributed to her multiple sclerosis.

III. Part 1: The Evidence Preponderates in Favor of Finding that Ms. Bravo Suffered from Multiple Sclerosis before the Vaccination

A. Health and Academic Record

Ms. Bravo was born in 1999. The medical records for her approximately first ten years appear not to contribute to the issues in this case. For more detailed information, See Pet'r's Br., filed July 1, 2021, at 10-11 and Resp't's Br., filed March 24, 2022, at 4-5.

When Ms. Bravo was nearly ten years old in 2009, she had problems with bedwetting, dysuria, incontinence, and constipation. Exhibit 3 at 67, 76. A renal ultrasound was normal. Id. at 87 (Aug. 20, 2009). A pediatric urologist stated that Ms. Bravo "holds her urine until it is too late and leaks," a phenomenon called "dysfunctional elimination syndrome." Id. at 108 (Sep. 3, 2009).

In Dr. Sriram's view, Ms. Bravo's problems with urination marked an initial presentation of the multiple sclerosis that was diagnosed years later. Exhibit C at 6-7. However, Dr. Steinman disagreed because urinary tract infections "are not uncommon in females." Exhibit 304 at 4.

Dr. Sriram also brought forward Ms. Bravo's academic record because "[c]ognitive changes and poor scholastic performance in schools are well recognized symptomology of [multiple sclerosis]." Exhibit C at 4. Dr. Sririam presented the following data:

Age	Year	Grade	Language	Math	Social Studies	Science
9	08-09	3	C+	C+	C	C+
10	09-10	4	C+	C-	B	B-
11	10-11	5	C+	C	B-	B+
12	11-12	6	C	F	F	C-
13	12-13*	7	C-	D	C-	D
14	13-14**	8	F	D	C-	F

Exhibit C at 3; see also Exhibit 5 at 2 (report card from elementary school). Although Dr. Steinman did not dispute that poor scholastic performance is associated with multiple sclerosis, he contended that "there are many causes for a change in scholastic performance." Exhibit 304 at 5.

The asterisk (*) in the chart reflects that Ms. Bravo received the first and second doses of the HPV vaccine during the 2012-2013 school year. Ms. Bravo's first dose was on October 3, 2012 during a routine "well teen" examination for a thirteen-year-old. Exhibit 3 at 274-76. She did not report any neurologic problems during this visit. Id.

The second HPV vaccination was given to Ms. Bravo on May 7, 2013. Exhibit 3 at 305-06. The context was a medical appointment during which Ms. Bravo complained about a tender lump on her left jawline, nausea after eating, and abdominal pain. Id. at 303-06. Ms. Bravo has not asserted that either the first dose or the second dose of the HPV vaccination harmed her.

The allegedly harmful dose was Ms. Bravo's third dose of the HPV vaccine, given during the 2013-2014 school year, marked with two asterisks (**) in the chart above. The date was March 21, 2014. Exhibit 3 at 370. On that date, she visited her pediatrician for a another "well teen" visit. Id. at 366. Her gross neurologic system was "normal by observation." Id. at 367. She was expected to return in about one year. Id. at 371.

Any plans for routine medical care were interrupted when Ms. Bravo began to experience pain in her right eye and intermittently blurry vision in later April 2014. She sought treatment at an emergency department on April 29, 2014. Exhibit 3 at 1477-79. She was determined to be neurologically intact and discharged. Id.

The next day, April 30, 2014, she returned to the emergency department and reported a two-to-three day history of right eye pain and headache. Exhibit 3 at 1481-84. She was directed to seek care from an ophthalmology clinic. Id.

An ophthalmologist determined that Ms. Bravo had difficulty with her vision and seeing color in her right eye. Exhibit 3 at 384-86 (May 1, 2014). The ophthalmologist diagnosed her with right retrobulbar neuritis and sent her to the hospital for an MRI. Id.

The hospitalization lasted from May 1 to May 10, 2014. Exhibit 3 at 1485-1601. Upon admission, a doctor obtained a history about her eye problems, consistent with the history recounted above. Id. at 1493. The doctor also

memorialized that Ms. Bravo "had a HPV vaccine 1 mo ago." Id. The doctor sought a consultation with a neurologist and ordered an MRI. Id. at 1497. The doctor was concerned that Ms. Bravo might suffer from a "demyelinating/autoimmune process (MS given female and age vs. ADEM.)" Id. at 1496.

The MRI, which presents critical information about when Ms. Bravo began to have lesions in her brain, was performed on May 2, 2014. The MRI revealed "5-10 scattered supratentorial areas of T2 signal hyperintensity within the white matter along the callosal-septal interface." Exhibit 3 at 1504. Some of the lesions did not enhance on contrast. Id. at 1583. As discussed below, experts retained in the litigation were provided the MRI images and commented upon them extensively.

By May 8, 2014, Ms. Bravo's doctors thought multiple sclerosis was likely. Exhibit 3 at 1574. This diagnosis was confirmed the next day.[3] Id. at 1583. She was treated with intravenous steroids, oral steroids, and plasmapheresis. She was discharged on May 10, 2014. Id. at 1593.

B. Procedural History regarding the Preexistence of Multiple Sclerosis

In his first report, Dr. Sriram opined that Ms. Bravo suffered from multiple sclerosis as early as 2008, based upon Ms. Bravo's dysuria, incontinence, and constipation. Exhibit C at 6. Dr. Sriram also relied upon imaging from Ms. Bravo's May 2, 2014 MRI. Exhibit C at 7-10.

After Dr. Sriram opined that Ms. Bravo suffered from multiple sclerosis before the vaccination, the parties discussed the viability of a significant

[3] Petitioner states that it is "a fundamental error" to base the analysis "on an agreed and uncontested medical diagnosis . . . of multiple sclerosis," because "[s]uch a diagnosis is rendered for purposes of [determining] methods of treatment of the existing disease process and not for determining the original etiological cause of the disease." Pet'r's Br. at 5. Petitioner further argues that "the actual basic underlying disease process from which [she] is suffering is a heterogenous auto-immune disease process which, when analyzed, presents with all of the disease process elements. Focusing the decision making process on multiple sclerosis may, and likely does, contribute to an erroneous determination of what was the nature of the original etiological agent of the scaring in the left side of [her] brain." Id. However, in both the original petition (filed April 10, 2017) and amended petition (filed November 16, 2018), petitioner alleged that she suffers "a cause in fact injury consisting of demyelinating disease process(s) known as optic neuritis and multiple sclerosis."

aggravation claim in a series of status conferences. After a discussion in an October 15, 2018 status conference, Ms. Bravo added a significant aggravation claim. Am. Pet., filed Nov. 16, 2018. However, Ms. Bravo did not present any evidence regarding significant aggravation, and counsel for petitioner maintained that the primary claim was for causation, and that the multiple sclerosis did not exist before the vaccination. See Order, issued July 29, 2019.

On January 23, 2020, the undersigned issued an order for briefs addressing whether Ms. Bravo suffered from multiple sclerosis before vaccination, noting that Ms. Bravo had not yet filed evidence on significant aggravation, and finding that she was thus pursuing a causation-in-fact claim only. Order, issued Jan. 23, 2020 at 7 n.4.

A status conference was held on February 6, 2020 to review the order. During the status conference, petitioner indicated that she wanted to proceed on a significant aggravation claim. See Order, issued Feb. 10, 2020. Ms. Bravo requested an opportunity to retain a neuroradiologist. Pet'r's Status Rep., filed Feb. 25, 2020. The Secretary did not oppose allowing Ms. Bravo "a final opportunity." Resp't's Status Rep., filed May 8, 2020.

The parties provided images of Ms. Bravo's MRIs to their experts in radiology and neuroradiology. For Ms. Bravo, Dr. Wilson wrote two reports. Exhibits 369 and 394. Dr. Steinman added a short report. Exhibit 400. For the Secretary, Dr. Kleefield wrote a report (Exhibit N) and Dr. Sriram wrote another report (Exhibit M).

After reviewing the evidence, the undersigned found that the evidence preponderated in favor of finding that a lesion detected in Ms. Bravo's brain was so old that it must have developed before she was vaccinated. This lesion was an unrecognized sign of multiple sclerosis. Thus, Ms. Bravo suffered from undiagnosed multiple sclerosis before the vaccination. Tentative Finding, issued Mar. 26, 2021.

After the Tentative Finding, the parties have not submitted any additional evidence regarding the onset of Ms. Bravo's multiple sclerosis. Nevertheless, Ms. Bravo challenges the Tentative Finding.

C. Analysis

Ms. Bravo's objections to the Tentative Finding can be placed into two categories. The first is procedural and the second is evidentiary.

1. Procedural

Ms. Bravo argues that special masters must base findings upon the entire record. Pet'r's Br. at 8. Although Ms. Bravo does not cite any authority for this proposition, the Vaccine Act says as much: special masters are to resolve cases based "on the record as a whole." 42 U.S.C. § 300aa–13(a)(1).

In this context, Ms. Bravo maintains "expert medical witness opinion testimony is required." Pet'r's Br. at 8. Although unstated, Ms. Bravo seems to be arguing that *oral* testimony is required. If this is Ms. Bravo's argument, then it is mistaken. Special masters may resolve entire cases without holding a hearing. Kreizenbeck v. Sec'y of Health & Hum. Servs., 945 F.3d 1362, 1365 (Fed. Cir. 2020). In doing so, special masters must consider the relevant evidence. Mager v. Sec'y of Health & Hum. Servs., 158 Fed. Cl. 136, 154 (2022). Here, the undersigned has considered all the evidence. Ms. Bravo's briefs filed after the Tentative Finding appear not to suggest that the undersigned overlooked any evidence. Instead, Ms. Bravo seems to be challenging the weight given to that evidence. This brings up Ms. Bravo's second objection to the Tentative Finding.

2. Evidentiary

In some respects, the evidence regarding the onset of Ms. Bravo's multiple sclerosis is confusing. But, in other and more important respects, the evidence is simple.

The confusing part derives from the report of Dr. Wilson. From Dr. Wilson's review of Ms. Bravo's original MRI images, he presented three examples of "acute demyelinating injury" in his Figure 1. Exhibit 369 at 3. Dr. Wilson also presented in his Figure 2 characteristics of the five largest lesions from Ms. Bravo's May 1, 2014 MRI. Id. at 4. However, Dr. Wilson does not state that the three lesions in Figure 1 correspond to the five lesions in Figure 2. See id.

In responding to Dr. Wilson, Dr. Kleefield asserts one of the three images in Figure 1 is an "artifact." Exhibit N at 3. But, Dr. Wilson maintained his position that the enhancement is "real." Exhibit 394 at 2-3.

To argue against the Tentative Finding, Ms. Bravo relies (in part) upon Dr. Kleefield's opinion regarding the "artifact." Pet'r's Br. at 7 and 9. In citing the opinion of the Secretary's expert, Ms. Bravo overlooks her own expert's argument that the image Dr. Wilson presented in Figure 1 shows an artifact. Exhibit 394 at 3 (Dr. Wilson: "I disagree with [Dr. Kleefield] that this lesion is artifactual.").

In any event, the three enhancements from Dr. Wilson's Figure 1 are not relevant. The key material is found in Dr. Wilson's Figure 2.

In Figure 2, Dr. Wilson identifies two lesions that lack enhancement. Exhibit 369 at 4; see also Exhibit M at 2 (Dr. Sriram: "Dr. Wilson 'states that there were 2 non-enhancing lesions seen on the MRI on 5/2/2014'"). These two non-enhancing lesions make the issue relatively easy. Dr. Sriram explained that one of the lesions, which can be described as being in the left frontal region or juxtacortical region, is a "hypo intense lesion" called a black hole. Exhibit M at 3; see also Exhibit N at 3-4; Frantz v. Sec'y of Health & Hum. Servs., No. 13-158V, 2019 WL 3713942, at *17 (Fed. Cl. Spec. Mstr. June 24, 2019) (discussing black holes), mot. for rev. denied, 146 Fed. Cl. 137 (2019). Due to the way black holes are created, the lesion must have existed before the vaccination. Exhibit M at 3-6. On this point, Dr. Wilson agrees. Exhibit 369 at 7; see also Exhibit 394 at 3 (Dr. Wilson stating "There is not major disagreement among experts in this case re: the chronicity of the discussed juxtacortical lesion").

With respect to the first of two non-enhanced lesions, Dr. Wilson is left in a challenging position. Having admitted the lesion pre-existed the vaccination, Dr. Wilson maintains the lesion is not related to multiple sclerosis. See Exhibit 369 at 4-5 and 7. This argument is difficult to sustain. Dr. Wilson states: "Juxtacortical lesions are seen in MS and may even be characteristic of MS." Exhibit 394 at 3. This statement aligns with Dr. Sriram's view. Exhibit M at 3-6.

Moreover, Dr. Sriram identifies a "weakly enhancing lesion in the left occipital trigone." Exhibit M at 9. Dr. Sriram also asserted that this lesion likely preexisted the vaccination due to its size (volume). Exhibit M at 7-8. Dr. Wilson does not meaningfully engage with Dr. Sriram on this point. See Exhibit 394 at 4.

Dr. Wilson states "there is no definitive MRI evidence that demyelinating disease preceded vaccination on 3/21/2014." Exhibit 394 at 1; see also Exhibit 369 at 6. The evidence probably is not "definitive." It might be a possibility that before the vaccination, Ms. Bravo could have had a lesion in her brain that was entirely separate from multiple sclerosis. However, the burden of proof is not "definitiveness." It is only preponderance. As Dr. Kleefield explained: "no one disagrees that the overwhelming majority of the lesions seen on MRI scans are typical for demyelinating disease. Therefore, such a diagnosis should also apply to the left frontal subcortical lesion, whose signal characteristics indicate it is a chronic abnormality preceding the vaccination date in question." Exhibit N at 4.

In addition to radiologic information about Ms. Bravo from her MRIs, other evidence supports a finding that she was, more likely than not, suffering from multiple sclerosis before vaccination. Dr. Sriram identified clinical and academic problems. Exhibit C at 6-7; see also Resp't's Br. at 5 n.9.[4] Dr. Steinman responded. Exhibit 304 at 4-5. As previously stated, this evidence is "not clear-cut." Tentative Finding at 2.[5]

3. Summary

The Tentative Finding cited two cases in which the (undersigned) special master found lesions pre-existed a vaccination. Tentative Finding at 2, citing W.C. v. Sec'y of Health & Hum. Servs., No. 07-456V, 2011 WL 4537877 (Fed. Cl. Spec. Mstr. Feb. 22, 2011), mot. for rev. denied in relevant part, 100 Fed. Cl. 440, 451-53 (2011), aff'd, 704 F.3d 1352 (Fed. Cir. 2013); Frantz v. Sec'y of Health & Hum. Servs., No. 13-158V, 2019 WL 3713942, at *17 (Fed. Cl. Spec. Mstr. June 24, 2019) (discussing black holes), mot. for rev. denied, 146 Fed. Cl. 137 (2019). Of this pair, W.C. carries the most weight due to the Federal Circuit's affirmance.

Other special masters have reached similar results. Maciel v. Sec'y of Health & Hum. Servs., No. 15-362V, 2018 WL 6259230, at *24 (Fed. Cl. Spec. Mstr. Oct. 12, 2018); L.Z v. Sec'y of Health & Hum. Servs., No. 14-920V, 2018 WL 5784525, at *17 (Fed. Cl. Spec. Mstr. Aug. 24, 2018). Ms. Bravo fails to address any of these precedents, including the two cases identified in the Tentative Finding.

Accordingly, to the extent required, the undersigned confirms the finding, which was tentative. A preponderance of the evidence supports the finding that Ms. Bravo had undiagnosed multiple sclerosis before the vaccination. Consequently, Ms. Bravo cannot prevail on a theory that the HPV vaccination was the cause-in-fact of her multiple sclerosis. Locane v. Sec'y of Health & Hum. Servs., 685 F.3d 1375, 1380-81 (Fed. Cir. 2012). She can, however, advance a claim that the HPV vaccination significantly aggravated the multiple sclerosis. As

[4] Dr. Sriram's opinion contradicts Ms. Bravo's assertion that in "unanimous agreement of the expert witnesses, [Ms. Bravo] was healthy with no clinical signs and symptoms of… multiple sclerosis." Pet'r's Br. at 11.

[5] Dr. Wilson's critiques of Dr. Sriram's assessment of the clinical picture in Ms. Bravo's case, Exhibit 369 at 6, are off base. As Dr. Wilson explained, neuroradiologists like him typically defer to practicing neurologists. Id.; see also Exhibit N at 1.

Dr. Wilson stated, "the immune challenge of a vaccine can worsen disease." Exhibit 394 at 3. That question is addressed next.

IV. Part 2 : The Evidence Does Not Preponderate in Favor of Finding the HPV Vaccine Significantly Aggravated Ms. Bravo's Multiple Sclerosis

A. Health

Ms. Bravo's health before her diagnosis with multiple sclerosis was set out above in section III.A. Following the third HPV vaccination, the parties basically agree about Ms. Bravo's health. See Pet'r's Br. at 21-23; Resp't's Br. at 7-10.

Once diagnosed with multiple sclerosis, Ms. Bravo explored a variety of treatments. During a relapse in July 2014, Ms. Bravo was tested for an infection with the Epstein-Barr virus. The results indicated that Ms. Bravo had a past infection. Exhibit 3 at 1374. Much later in the litigation, Dr. Romberg opined that the infection with the Epstein-Barr virus was a better explanation for why she developed multiple sclerosis. Exhibit V. In response, Dr. Steinman maintained that an infection with the Epstein-Barr virus was necessary but not sufficient to cause multiple sclerosis. Exhibit 427.

Otherwise, the remaining medical records seem not to inform the issue of whether the HPV vaccination worsened Ms. Bravo's multiple sclerosis. See Pet'r's Br. at 23 (summarizing two and half years of medical records in two paragraphs). Thus, they are not written about here, although those recent medical records have been considered.

B. Procedural History

Setting aside Dr. Wilson, whose role was to comment on radiologic evidence, Ms. Bravo presented reports from four people. These are: Dr. Steinman, Dr. Shoenfeld, Dr. Lee, and Dr. Shaw. The Secretary filed reports from Dr. Sriram and Dr. Romberg, again excepting the neuroradiologist (Dr. Kleefield).

1. Dr. Shaw and Dr. Lee

It appears that Ms. Bravo is relying upon Dr. Steinman and Dr. Shoenfeld exclusively and not relying upon either Dr. Lee or Dr. Shaw. Other than a discussion of the qualifications of Dr. Lee and Dr. Shaw, Ms. Bravo does not advance their opinions. See Pet'r's Br. at 18-19. The Secretary also understood that Ms. Bravo was not relying upon opinions from either Dr. Lee or Dr. Shaw. Resp't's Br. at 24 n.24. Ms. Bravo, in turn, did not correct any misunderstanding

or otherwise argue for opinions from Dr. Lee or Dr. Shaw. See Pet'r's Reply, filed April 8, 2022 and Pet'r's Supplemental Reply, filed May 4, 2022.

Nevertheless, if only to confirm that Dr. Shaw's and Dr. Lee's opinions have been considered, they are addressed briefly.

a) Dr. Lee

Dr. Lee wrote four reports, which were filed as Exhibits 92, 251, 325 and 352. A fifth report (Exhibit 166) revised Dr. Lee's original report (Exhibit 92). In his final two reports, Dr. Lee addressed, among other topics, an epidemiological study by Scheller. Exhibits 325, 352.

A general thrust of Dr. Lee's opinion is that the HPV vaccine acts as a TLR9 agonist and that TLR9 activates cells of the innate immune system to cause multiple sclerosis. See, e.g., Exhibit 251 at 9, 30. Dr. Lee contends that the HPV vaccines "contain a significant quantity" of HPV DNA fragments bound to amorphous aluminum hydroxyphosphate sulfate ("AAHS"), acting as a "silent TLR9 agonist." Id. at 28. However, as previously stated, it appears that Ms. Bravo is not advancing this theory because, at best, she quoted one paragraph of one report from Dr. Lee in her brief. Pet'r's Br. at 19. This limited quotation does not comply with the requirement that the parties should not simply quote from an expert's report. Order for Briefs, filed March 26, 2021, at 6.

In any event, Dr. Romberg has undermined the persuasive value of a theory based upon TLR9 in his reports. Dr. Romberg points out that the Zannetti study,[6] which Dr. Lee cites, does not prove that the HPV vaccine is a TLR9 agonist, but rather, suggests that a significant portion of the activating effect is unrelated to TLR9 activation. Exhibit F at 2. Dr. Romberg further notes that Dr. Lee's estimate that "a significant quantity" of HPV DNA is bound by AAHS is not a quantitative estimate, and is based only on Dr. Lee's own experiments using a technique which cannot quantitate DNA. Id. at 2-3. "[I]n summary . . . both the quantity of DNA in Gardasil and its ability to activate TLR9 remain fully in question." Id.; see also Exhibit H at 1-2. Moreover, one special master persuasively found that Dr. Lee's presentation of a TLR9 theory was not persuasive. E.S. v. Sec'y of Health & Hum. Servs., No. 17-480V, 2020 WL 9076620, at *50 (Fed. Cl. Spec. Mstr. Nov. 13, 2020) (noting that Dr. Lee had not presented any persuasive or reliable literature, but had "only proposed that general research he had performed was enough."), mot. for rev. denied, 154 Fed. Cl. 149

[6] Bibliographic information for the articles cited in this decision is found in the appendix.

(2021); c.f. Aviles v. Blasio, No. 20 Civ. 9829, 2021 WL 796033, at *14 (S.D.N.Y. Mar. 2, 2021) (describing one of Dr. Lee's opinions as "rank speculation").

Under these circumstances an extended discussion of Dr. Lee's background and his opinions is unnecessary. It suffices to state that they are not persuasive. Cf. Roane v. McDonough, 64 F.4th 1306, 1309 (Fed. Cir. 2023) (explaining that the Board of Veterans' Appeals is not required to explain how each piece of evidence factored into its decision).

b) Dr. Shaw

Dr. Shaw drafted three reports. Exhibits 30, 132 (one-page), and 296. He appears to be asserting that Ms. Bravo's case represents an example of an Autoimmune Syndrome Induced by Adjuvants ("ASIA").

Ms. Bravo pays even less attention to reports from Dr. Shaw. She did not quote his report or otherwise cite to them. At best, Ms. Bravo references the ASIA theory in the context of Dr. Shoenfeld. Pet'r's Br. at 12.

Accordingly, it appears that the reports from Dr. Shaw carry little, if any, independent weight. To the extent that Dr. Shaw is asserting ASIA, special masters have consistently rejected ASIA. See, e.g., Rowan v. Sec'y of Health & Hum. Servs., 2015 WL 3562409 (Fed. Cl. May 18, 2015) (denying motion for review and ruling special master did not err in not crediting ASIA); Phillips v. Sec'y of Health & Hum. Servs., No. 16-906V, 2020 WL 7767511 (Fed. Cl. Spec. Mstr. Nov. 23, 2020); Pearson v. Sec'y of Health & Hum. Servs., No. 16-9V, 2019 WL 3852633 (Fed. Cl. Spec. Mstr. July 31, 2019). The undersigned agrees with the reasoning in these cases, and Ms. Bravo has presented no reason—let alone a persuasive reason—for reconsidering those outcomes. See Pet'r's Supp'l Br. at 3. To the extent that Dr. Shaw is supporting Dr. Shoenfeld's opinions, Dr. Shaw's work is considered in the context of Dr. Shoenfeld.

2. Dr. Shoenfeld

Unlike the situation for Dr. Lee and Dr. Shaw, in which Ms. Bravo appears to have disclaimed any reliance upon them, Ms. Bravo is certainly putting forward the opinions of Dr. Shoenfeld. Thus, the disclosure of Dr. Shoenfeld's opinions and the Secretary's responses to those opinions are discussed in more detail.

Dr. Shoenfeld's First Report. Dr. Shoenfeld's first report is fourteen pages plus an additional page listing 19 references. Exhibit 9.[7] After some preliminary matters, including a review of his qualifications and the facts of Ms. Bravo's case, Dr. Shoenfeld discussed a few case reports in which the HPV vaccine preceded the development of a different autoimmune disease, neuromyelitis optica ("NMO"). Id. at 7-10.

For theories by which the HPV vaccine can cause harmful consequences, Dr. Shoenfeld offered two possibilities. First, Dr. Shoenfeld emphasized that the adjuvant for the HPV vaccine could persist leading to "delayed neurotoxicity." Id. at 10. In this context, Dr. Shoenfeld explained that aluminum has been found in a condition known as macrophagic myofasciitis. Id. at 10-11. Second, Dr. Shoenfeld suggested that the adjuvant could augment a reaction driven by molecular mimicry as Dr. Steinman has proposed. Id. at 11-12.

Dr. Shoenfeld's Second Report. In response to an order seeking clarification from Dr. Shoenfeld, Dr. Shoenfeld wrote a second report, which is dated February 5, 2018, and filed as Exhibit 142. He stated that aluminum is associated with demyelinating diseases and aluminum can accumulate in the brain. Exhibit 142 at 2-3.

Dr. Romberg's First Report. Dr. Romberg opined that, based upon an epidemiologic study (Scheller), the HPV vaccine was unlikely to cause or to worsen multiple sclerosis. Exhibit A at 14. In response to Dr. Shaw, Dr. Romberg presented information about the hemodialysis of aluminum and the amount of aluminum contained in an HPV vaccine. Id. at 15. Dr. Romberg disputed the potential harmful nature of aluminum by citing a large epidemiologic study (Linneberg). Id.

Dr. Sriram's First Report. Dr. Sriram maintained that the case reports on NMO did not inform the question of multiple sclerosis. Exhibit C at 11. Dr. Sriram also noted that one of the studies Dr. Shoenfeld had cited (referenced by Dr. Shoenfeld as the study by "Brocke and colleagues" but cited as Ufret-Vincenty et al., Exhibit 9 at 12, 15) was not about the HPV vaccine, but was about the Epstein-Barr virus. Id. at 12. Finally, Dr. Sriram opined that no evidence shows aluminum in vaccines causes multiple sclerosis. Id. at 13.

[7] This first report was essentially refiled as Exhibit 324. See CM/ECF 72.

Dr. Shoenfeld's Third Report. In Dr. Shoenfeld's third report, he briefly responded to Dr. Romberg's citation to the Scheller epidemiologic study. Exhibit 311.

Dr. Shoenfeld's Fourth Report. Dr. Shoenfeld responded to Dr. Sriram's report by extending his discussion of molecular mimicry and Kanduc. Exhibit 314 at 3-5.[8] Dr. Shoenfeld offered the idea that multiple sclerosis could be aggravated due to hyper-stimulation of the immune system by the HPV vaccine. Id. at 5 (citing, among other articles, a 2009 article by Kanduc and a 2016 article by Kanduc and Shoenfeld).

Dr. Romberg's Second Report. This report did not direct any comments to Dr. Shoenfeld. However, with respect to the issue of aluminum toxicity raised by Dr. Shaw, Dr. Romberg again cited the Danish study. Exhibit F at 6.

Dr. Sriram's Second Report. Dr. Sriram continued to disagree with Dr. Shoenfeld's reliance on case reports involving demyelinating diseases other than multiple sclerosis because, in Dr. Sriram's view, demyelinating diseases have different etiologies. Exhibit G at 6.

Dr. Shoenfeld's Fifth and Sixth Reports. Dr. Shoenfeld's fifth report generally concerned the question of onset. Exhibit 342.

In his sixth report, Dr. Shoenfeld responded to Dr. Romberg's preference for looking at epidemiologic studies by highlighting the need to look at animal models. Exhibit 344 at 1. In this context, Dr. Shoenfeld cited an article by Inbar, which was filed as Exhibit 346.

3. Dr. Steinman

Like Dr. Shoenfeld, Dr. Steinman wrote a series of reports to which Dr. Sriram and Dr. Romberg responded. A summary of their respective positions is as follows:

Dr. Steinman's First Report. Dr. Steinman began his first report with a summary of his qualifications and a recitation of Ms. Bravo's medical history. Exhibit 70 at 1-7. Dr. Steinman then proposed two different theories by which an HPV vaccination might affect multiple sclerosis. The first theory is molecular

[8] Dr. Shoenfeld and Dr. Sriram also debated the onset of Ms. Bravo's multiple sclerosis. Because the previous section resolved this issue, these exchanges are not detailed here.

mimicry based upon BLAST searches. Id. at 8-20. Dr. Steinman conducted these BLAST searches despite not knowing the dominant antigen associated with multiple sclerosis. See id. at 8-10. The second theory involves alum[9] and was presented in approximately two paragraphs. Id. at 20. His section on timing (section 6) was based upon an assertion that the HPV vaccine caused Ms. Bravo's multiple sclerosis. Id. at 20-21. Dr. Steinman did not state when the multiple sclerosis began. See id. at 22. Finally, in the section on the logical sequence of cause and effect (section 7), Dr. Steinman did not say anything about Ms. Bravo. Id. at 22.

Dr. Steinman's Second Report. In response to a February 27, 2018 order, Dr. Steinman presented additional support for his theory involving alum. Dr. Steinman asserted that alum adjuvants induce a cytokine, known as IL-1beta. IL-1beta, according to Dr. Steinman, "has a critical role in the pathogenesis of [multiple sclerosis]." Exhibit 133 at 5.

Dr. Romberg's First Report. In addressing Dr. Lee's opinions, Dr. Romberg cited the Scheller epidemiologic study. Exhibit A at 10-11. Dr. Romberg also addressed Dr. Steinman's alum theory and his molecular mimicry theory. Id. at 12.

Dr. Sriram's First Report. Although Dr. Steinman's BLAST searches involved myelin basic protein and myelin oligodendrocyte-glycoprotein, Dr. Sriram maintained that those substances have not been implicated in the pathology of multiple sclerosis. Exhibit C at 13.

Dr. Steinman's Third Report. Dr. Steinman responded to both Dr. Romberg and Dr. Sriram in a single report. For Dr. Romberg, Dr. Steinman asserted that alum in the vaccine boosts the response from the immune system. Exhibit 304 at 1. For Dr. Sriram, Dr. Steinman argued that Ms. Bravo must have some genetic susceptibility to developing an adverse reaction to the HPV vaccine. Id. at 4.[10]

[9] Alum is short for "aluminum adjuvants," and is a component in the Gardasil vaccine. Exhibit 133 at 1; see also Gross v. Sec'y of Health & Hum. Servs., No. 17-1075V, 2022 WL 9669651, at *17 n.59 (Fed. Cl. Sept. 22, 2022).

[10] As with Dr. Shoenfeld, Dr. Steinman also contributed opinions as to when Ms. Bravo began suffering from multiple sclerosis. See, e.g., Exhibit 304 at 5-6. But, again, the details are omitted from this discussion on significant aggravation.

Dr. Romberg's Second Report. Dr. Romberg argued that the HPV virus evades detection from the immune system. Thus, alum does not boost the immune response. Exhibit F at 7-8.

Dr. Steinman's Fourth Report. To support his theory involving molecular mimicry, Dr. Steinman relied upon information he gained from consulting the immune epitope database. Exhibit 349 at 2-8. Dr. Steinman also proposed that Ms. Bravo might establish the HPV vaccine significantly aggravated her multiple sclerosis. Id. at 12. In the context of reviewing the six Loving prongs, Dr. Steinman's section about the logical sequence of cause and effect was one sentence. Id. at 13.

Dr. Romberg's Third Report. Dr. Romberg disagreed with how Dr. Steinman was using the immune epitope database. Exhibit H at 3. Also, in the context of responding to Dr. Lee, Dr. Romberg cited another epidemiologic study, Klein. Id.

Dr. Steinman's Sixth Report.[11] In the briefing stage, Dr. Steinman presented two new papers (by Robinson & Steinman and Lanz et al.) about the potential role of Epstein-Barr viruses causing multiple sclerosis. Exhibit 414, dated April 29, 2022.

Dr. Romberg's Fourth Report. Based upon Dr. Steinman's most recent report, Dr. Romberg proposed that an Epstein-Barr infection was a better explanation for Ms. Bravo's multiple sclerosis. Exhibit V.

Dr. Steinman's Seventh Report. Dr. Steinman asserted that the recent studies indicate that an infection with Epstein-Barr virus is necessary, but not sufficient, to cause multiple sclerosis. Another factor is needed and in Ms. Bravo's case the additional factor was the HPV vaccination. Exhibit 427.

C. Elements of Significant Aggravation

As confirmed in W.C. v. Sec'y of Health & Human Servs., 704 F.3d 1352, 1357 (Fed. Cir. 2013), the elements of an off-Table significant aggravation case were stated in Loving. There, the Court blended the test from Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274, 1279 (Fed. Cir. 2005), which defines off-Table causation cases, with a test from Whitecotton v. Sec'y of Health & Human

[11] Dr. Steinman's fifth report commented on the reports submitted by neuroradiologists after reviewing Ms. Bravo's MRIs. Exhibit 400.

Servs., 81 F.3d 1099, 1107 (Fed. Cir. 1996), which concerns on-Table significant aggravation cases. The resulting test has six components. These are:

> (1) the person's condition prior to administration of the vaccine, (2) the person's current condition (or the condition following the vaccination if that is also pertinent), (3) whether the person's current condition constitutes a "significant aggravation" of the person's condition prior to vaccination, (4) a medical theory causally connecting such a significantly worsened condition to the vaccination, (5) a logical sequence of cause and effect showing that the vaccination was the reason for the significant aggravation, and (6) a showing of a proximate temporal relationship between the vaccination and the significant aggravation.

Loving, 86 Fed. Cl. at 144.

D. Analysis

In resolving claims of significant aggravation, special masters may focus their analysis on the last three prongs of the Loving test, which correspond to the traditional Althen factors. Walker v. Sec'y of Health & Hum. Servs., No. 18-299V, 2022 WL 11141194, at *3 (Fed. Cl. Spec. Mstr. Sep. 27, 2022) (citing Hennessey v. Sec'y of Health & Hum. Servs., No. 01-190V, 2009 WL 1709053, at *42 (Fed. Cl. Spec. Mstr. May 29, 2009), mot. for rev. denied, 91 Fed. Cl. 126 (2010)).

1. Loving Prong 4 / Althen Prong 1

Ms. Bravo's burden is to present a reliable and persuasive medical theory. Faup v. Sec'y of Health & Hum. Servs., 147 Fed. Cl. 445, 459 (2019) (citing Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351, 1360 (Fed. Cir. 2019) and Knudsen v. Sec'y of Health & Hum. Servs., 35 F.3d 543, 548 (Fed. Cir. 1994)). The Secretary may controvert the evidence Ms. Bravo submits. de Bazan v. Sec'y of Health & Hum. Servs., 539 F.3d 1347, 1353–54 (Fed. Cir. 2008).

When the Secretary challenges a petitioner's Althen prong one evidence, a special master is not required to find the petitioner automatically has met the burden regarding a causal theory. M.S.B. by Bast v. Sec'y of Health & Hum. Servs., 117 Fed. Cl. 104, 123 (2014) (ruling special master was not arbitrary in rejecting a theory of oxidative stress and noting that the Federal Circuit has determined the special masters are responsible for assessing "conflicting testimony of expert witnesses in determining whether a reputable theory has been proven"),

appeal dismissed, 579 Fed. App'x 1001 (Fed. Cir. 2014); Spates v. Sec'y of Health & Hum. Servs., 76 Fed. Cl. 678, 684 (2007).

As explained above, Ms. Bravo maintains that she is putting forward two theories. "There are two generally accepted medical theories as to the original etiological cause of an autoimmune disease due to [an HPV vaccination]. . . . One is the mimicry theory and the second is the ASIA theory developed by Petitioner's expert witness Dr. Yehuda Shoenfeld." Pet'r's Br. at 12. Ms. Bravo elaborates: "The two theories are essentially the same with ASIA in name identifying the specific causal factor as an adjuvant." Id.

However, Ms. Bravo's characterization of her experts' theories is mistaken. Dr. Shoenfeld proposes that alum accumulates in the brain and causes neurotoxicity. Exhibit 9 at 10-11; Exhibit 142 at 3. In these reports, Dr. Shoenfeld does not discuss any cytokines and he does not talk about IL-1beta. In contrast, Dr. Steinman proposes that alum leads to a creation of and/or activation of IL-1beta and IL-1beta leads to multiple sclerosis. Exhibit 133 at 5. Dr. Steinman does not assert that alum persists. Thus, although Dr. Shoenfeld and Dr. Steinman propose theories that start with alum, each theory proceeds differently.

To be sure, Dr. Steinman and Dr. Shoenfeld slightly overlap with respect to the remaining theory, molecular mimicry. Dr. Steinman proposes that certain sequences of amino acids in the HPV vaccine resemble (or mimic) sequences of amino acids in proteins of the nervous system, myelin basic protein and myelin oligodendrocyte-glycoprotein. Exhibit 70 at 10. Dr. Shoenfeld, but not Dr. Steinman, adds that the alum in the HPV vaccination can hyper-stimulate the immune system. Exhibit 314 at 5. At no point did Dr. Steinman assert that the part of the HPV vaccine that serves as the foundation for his theory of molecular mimicry is found in the adjuvant.

Accordingly, *three* theories are evaluated below. They are the persistence of alum causing neurotoxicity, alum leading to IL-1beta, and molecular mimicry. Because Ms. Bravo devotes most attention to molecular mimicry, see Pet'r's Br. at 12-13; Pet'r's Supp'l Br. at 3-5, and Pet'r's Reply at 4-5; that theory is considered most extensively. Before those individual theories are detailed, an assessment of the epidemiologic evidence the Secretary submitted begins the overall analysis.

a) Epidemiology

Epidemiology is a method by which medical researchers determine whether an exposure to a substance changes the incidence of a condition. For example,

when Dr. Steinman was assisting this country on a committee in evaluating whether veterans who served in the Gulf War developed various diseases at higher rates, Dr. Steinman and other committee members considered whether epidemiologic evidence would be useful. Exhibit 72. For a lengthy discussion of the value of epidemiologic studies in the Vaccine Program, see Tullio v. Sec'y of Health & Human Servs., No. 15-51V, 2019 WL 7580149, at *5-8 (Fed. Cl. Spec. Mstr. Dec. 19, 2019), mot. for rev. denied, 149 Fed. Cl. 448, 475 (2020); see also P.M. v. Sec'y of Health & Hum. Servs., No. 16-949V, 2019 WL 5608859, at *24-25 (Fed. Cl. Spec. Mstr. Sep. 24, 2019) (finding that epidemiologic studies weighed against finding the flu vaccine can worsen multiple sclerosis).

Among the hundreds of articles filed, two epidemiologic studies stand out and a third merits some discussion. The first is by Nikolai Madrid Scheller and others. Exhibit A-12. The second is by Julie Mouchet and others. Exhibit C-4. The third is by Nicola Klein and others. Exhibit H-2.

The Scheller group "conducted a cohort study of all Danish and Swedish girls and women aged 10 years to 44 years on the basis of nationwide registers and investigated the risk of multiple sclerosis and other demyelinating diseases … following qHPV vaccination." Scheller at 55.[12] The study involved nearly four million females, among whom 789,082 people received nearly two million doses of the vaccine. Because multiple sclerosis may have an insidious onset, the researchers considered a "2-year (730 days) risk period following the latest qHPV vaccination." Id. at 56. The researchers found that the adjusted risk ratio was 1.01 with a 95% confidence interval of 0.76-1.34. Id. at 59. They concluded that "qHPV vaccination, among girls and women, was not associated with the development of multiple sclerosis" and their findings "do not support concerns about a causal relationship between qHPV vaccination and demyelinating diseases." Id. at 60.

The Scheller study was incorporated into the Mouchet analysis, which is the second important epidemiologic study. Mouchet and colleagues conducted a meta-analysis of studies involving the HPV vaccine and various demyelinating diseases, including multiple sclerosis. For multiple sclerosis, the investigator evaluated six studies (including Scheller, which is reference 42 in the Mouchet article). Mouchet at 114. The number of people receiving a vaccination in the pooled group exceeded two million, with the Scheller article contributing approximately

[12] The qHPV vaccine analyzed in Scheller is the same vaccine that Ms. Bravo received.

half. Id. at 115 (Fig. 3). "The pooled risk ratio obtained by the meta-analysis was 0.98" with a 95% confidence interval of 0.82-1.19. Id. at 114.

The Mouchet group concluded that their study and other studies "plead[] for an incidental association between vaccination and demyelination rather than a causal relationship." They also went a step further to say: "These data do not support the interesting hypothesis . . . regarding a biological plausibility based upon a molecular mimicry of the vaccine with myelin basic protein." Id. at 115.

The final study is by Klein and colleagues and was performed in 2012. These researchers looked at people in the Kaiser Permanente system in California. They found that the incidence of a hospital visit for a disease of the nervous system did not meaningfully increase after a dose of the HPV vaccine. Klein at 1143 (table 2). However, the broad category of "diseases of the nervous system" is not as specific as multiple sclerosis, which was studied in Scheller and Mouchet.

Two of Ms. Bravo's experts criticized the Scheller study. Dr. Shoenfeld preferred case reports to epidemiologic studies. Exhibit 311 at 1. However, case reports contribute little, if anything, to evaluating claims of causation. See K.O. v. Sec'y of Health & Human Servs., No. 13-472V, 2016 WL 7634491, at *11-12 (Fed. Cl. Spec. Mstr. July 7, 2016) (discussing appellate precedent on case reports). For this reason, articles presenting case reports of multiple sclerosis are not discussed here. See, e.g., Sutton (Exhibit 317).[13]

Dr. Lee took issue with the Scheller study and the Klein study. Exhibit 325 at 15, Exhibit 352 at 5-8. However, Dr. Lee's curriculum vitae does not suggest that he has expertise in epidemiology. See Exhibit 93.

Overall, these epidemiologic studies tend to undermine any claim that the HPV vaccination either causes or aggravates multiple sclerosis. Special masters have cited these studies in finding that the evidence did not preponderate in favor of finding that the HPV vaccine can cause or worsen multiple sclerosis. See Heddens v. Sec'y of Health & Hum. Servs., No. 15-734V, 2018 WL 5726991, at

[13] Even further afield are case reports of demyelinating diseases other than multiple sclerosis. As Dr. Sriram stated, "ADEM and NMO are two different diseases and are treated differently from MS." Exhibit C at 12. Dr. Sriram's view is corroborated by Mouchet and others. In their meta-analysis, "Each neurological event (i.e., broad category of central demyelination, ([multiple sclerosis, optic neuritis, Guillain-Barré syndrome]) was considered separately, since the biological mechanisms leading to these events have little in common." Mouchet at 112.

*3 (Fed. Cl. Spec. Mstr. Oct. 5, 2018) mot. for rev. denied, 143 Fed. Cl. 193 (2019); Maciel v. Sec'y of Health & Hum. Servs., No. 15-362V, 2018 WL 6259230, at *14, *27 (Fed. Cl. Spec. Mstr. Oct. 12, 2018).

However, epidemiology cannot prove a negative. Therefore, the three methods about which Dr. Shoenfeld and Dr. Steinman have opined are addressed.

b) Persistence of Alum and Neurotoxicity

As previously stated, special masters have consistently not credited a theory that adjuvants, such as alum, induce an autoimmune disease. Differentiating Dr. Shoenfeld's current theory from the theory he has expressed in other cases seems difficult. While Ms. Bravo asserts that "Dr. Shoenfeld . . . did not assert ASIA," (Pet'r's Supp'l Br. at 3), Dr. Shoenfeld presents a theory based upon alum. See Exhibit 9 at 10-11.

Regardless of whether Ms. Bravo has actually disclaimed this theory, the Secretary's experts easily refuted it. For example, Dr. Romberg relied upon a large study investigating how people exposed to aluminum respond. Exhibit A at 15, Exhibit F at 6.

In this study, Allan Linneberg and colleagues investigated whether Danish people who received subcutaneous allergen-specific immunotherapy developed autoimmune diseases at an increased rate compared with Danish people who received a different type of allergy treatment. Linneberg, Exhibit A-25. The subcutaneous allergen-specific immunotherapy "contains aluminum hydroxide as an adjuvant for depot vaccination." Id. at 418. One disease specifically investigated was multiple sclerosis. Id. at 415 (Table 1). The people who received this therapy were at a slightly lower risk for developing an autoimmune disease. The hazard ratio was 0.86 with a 95% confidence interval of 0.74-0.99. Id. at 413. Thus, the Linneberg article tends to undermine the theory that exposure to aluminum is likely to cause multiple sclerosis.

The next significant flaw in the theory that aluminum from the HPV vaccine can cause neurotoxicity concerns the amount of aluminum in a vaccine. Dr. Romberg presented information about the amount of aluminum contained in an HPV vaccine and the hemodialysis of aluminum. Exhibit A at 15. Essentially, an HPV vaccine includes an amount of aluminum much smaller than the amounts given to mice in experiments that potentially show the harmful effect of aluminum. Id. at 15-16. As Dr. Romberg states: "Even seemingly innocuous substances like water or milk can be toxic if ingested in large amounts." Special masters have

reached the same conclusion. See Spahn v. Sec'y of Health & Hum. Servs., No. 09-386V, 2014 WL 12721080, at *17 (Fed. Cl. Spec. Mstr. Sep. 11, 2014), mot. for rev. denied, 133 Fed. Cl. 588, 603 (2017); Snyder v. Sec'y of Health & Hum. Servs., No. 01-162V, 2009 WL 332044, at *65 (Fed. Cl. Spec. Mstr. Feb. 12, 2009), mot. for rev. denied, 88 Fed. Cl. 706 (2009). The undersigned agrees with the reasoning in these cases.

Finally, no persuasive evidence shows that aluminum in vaccines causes multiple sclerosis. See Exhibit C (Dr. Sriram's report) at 13.

In light of the above, Ms. Bravo has not met her burden of establishing that the persistence of aluminum can lead to multiple sclerosis.

c) Alum Leading to IL-1beta

The next potential theory comes from Dr. Steinman, who asserted that the alum component of the vaccine induces the production of a cytokine (IL-1beta) and this cytokine contributes to the propagation of multiple sclerosis. See, e.g., Exhibit 133. Preliminarily, it must be pointed out (again) that whether Ms. Bravo continues to put forward this theory is doubtful. None of her four briefs submitted in advance of potential adjudication contain the term "cytokine" or "IL-1beta." Thus, Ms. Bravo could be found to have waived this theory. See Vaccine Rule 8(f).

Because Dr. Steinman's theory based on alum involves aluminum, the Linneberg article is an obstacle. As just explained, people who were exposed to aluminum in that study did not develop any autoimmune disease (including multiple sclerosis) at an increased rate. Likewise, Dr. Steinman appears not to have accounted for the dose of alum and the body's process for responding to it.

Special masters have generally, but not always, found theories based upon cytokines causing harm unpersuasive. See, e.g., O.M.V. v. Sec'y of Health & Hum. Servs., No. 16-1505V, 2021 WL 3183719, at *43-46 (Fed. Cl. Spec. Mstr. June 6, 2021) (flu vaccine not shown to cause multiple sclerosis or acute disseminated encephalomyelitis), mot. for rev. denied, 2021 WL 6124731 (Fed. Cl. 2021); Rupert v. Sec'y of Health & Hum. Servs., No. 15-841V, 2021 WL 1832909, at *36-39 (Fed. Cl. Spec. Mstr. May 1, 2021) (flu vaccine was not shown to aggravate glomerulonephritis); McKown v. Sec'y of Health & Hum. Servs., No. 15-1451V, 2019 WL 4072113, at *50 (Fed. Cl. Spec. Mstr. July 15, 2019) (finding that an HPV vaccine was not shown to cause postural tachycardia syndrome, stating that the "fact that cytokine upregulation is promoted by vaccination – a

medically reliable assertion standing alone – does not mean that this cytokine increase is definitionally *harmful*," and rejecting ASIA theory); But see Switzer v. Sec'y of Health & Hum. Servs., No. 18-1418V, 2022 WL 4482721, at *17 (Fed. Cl. Spec. Mstr. Aug. 29, 2022) (flu vaccine and pneumococcal conjugate vaccines shown to cause systemic inflammatory response syndrome).

In other cases, special masters have rejected the theories based upon alum. Samuels v. Sec'y of Health & Hum. Servs., No. 17-071V, 2020 WL 2954953, at *20 (Fed. Cl. Spec. Mstr. May 1, 2020) (not crediting Dr. Steinman's opinion that the Tdap vaccine can cause multiple sclerosis or acute disseminated encephalomyelitis and indicating that Dr. Steinman's alum theory was close to the discredited ASIA theory); Zumwalt v. Sec'y of Health & Hum. Servs., No. 16-994V, 2019 WL 1953739, at *18 (Fed. Cl. Spec. Mstr. Mar. 21, 2019) (not crediting Dr. Steinman's theory that alum adjuvant in DTaP played a role in causing petitioner's seizures), mot. for rev. denied, 146 Fed. Cl. 525, 539-40 (2019). The undersigned agrees with the reasoning in these decisions, and Ms. Bravo has not presented any persuasive evidence that theories based upon alum are reliable.

Under the circumstances in which Ms. Bravo has not meaningfully advanced this theory, evidence contrary to the theory is in the record, and the caselaw trends against the theory, a more elaborate discussion is not required. Ms. Bravo has not established the persuasiveness of the theory that alum worsens (or causes) multiple sclerosis.

d) Molecular Mimicry

A more detailed discussion, however, is appropriate for the last theory. Ms. Bravo has indisputably advanced molecular mimicry to explain how an HPV vaccination can aggravate multiple sclerosis.

Because special masters are often called upon to evaluate the persuasiveness of the theory of molecular mimicry, the Court of Federal Claims and the Court of Appeals for the Federal Circuit have considered molecular mimicry in their appellate role. In December 2019, the undersigned identified the leading precedents as W.C. v. Sec'y of Health & Hum. Servs., 704 F.3d 1352 (Fed. Cir. 2013), and Caves v. Sec'y of Dep't. of Health & Hum. Servs., 100 Fed. Cl. 119 (2011), aff'd sub nom., 463 F. App'x 932 (Fed. Cir. 2012). Tullio v. Sec'y of Health & Hum. Servs., No. 15-51V, 2019 WL 7580149, at *12-14 (Fed. Cl. Spec. Mstr. Dec. 19, 2019), mot. for rev. denied, 149 Fed. Cl. 448 (2020). While Tullio describes those cases in more detail, their essence appears to be that although

molecular mimicry is accepted in some contexts, special masters may properly require some empirical evidence to show that a particular vaccine can cause a particular disease.

In the next approximately three years, appellate authorities reviewing decisions involving molecular mimicry have generally endorsed the approach of looking for some evidence that persuasively shows that a portion of a vaccine resembles a portion of human tissue, which contributes to causing the disease, and that the immune system will respond to the relevant amino acid sequence.[14] Chronologically, the list of more recent appellate cases begins with the opinion in Tullio, which denied the motion for review. 149 Fed. Cl. 448, 467-68 (2020).

Another example in which the Court of Federal Claims held that the special master did not elevate the petitioner's burden of proof in the context of evaluating the theory of molecular mimicry is Morgan v. Sec'y of Health & Hum. Servs., 148 Fed. Cl. 454, 476-77 (2020), aff'd in non-precedential opinion, 850 F. App'x 775 (Fed. Cir. 2021). In Morgan, the Chief Special Master found that petitioner had not presented persuasive evidence about a relevant antibody. Id. at 477. The Chief Special Master also noted that the articles about the relevant disease do not list the wild flu virus as potentially causing the disease. Id. When examining this analysis, the Court of Federal Claims concluded: "the Chief Special Master did not raise the burden of causation in this case; petitioner simply failed to meet it." Id.

The Federal Circuit also evaluated the Chief Special Master's approach in Morgan. The Federal Circuit concluded: "We discern no error in the special master's causation analysis." 850 F. App'x 775, 784 (Fed. Cir. 2021).

Most other recent appellate cases follow this path. See, e.g., Duncan v. Sec'y of Health & Hum. Servs., 153 Fed. Cl. 642, 661 (2021) (finding the special master did not err in rejecting a bare assertion of molecular mimicry); Caredio v. Sec'y of Health & Hum. Servs., No. 17-79V, 2021 WL 6058835, at *11 (Fed. Cl. Dec. 3, 2021) (indicating that a special master did not err in requiring more than homology and citing Tullio); Yalacki v. Sec'y of Health & Hum. Servs., 146 Fed. Cl. 80, 91-92 (2019) (ruling that special master did not err in looking for reliable evidence to support molecular mimicry as a theory); but see Patton v. Sec'y of Health & Hum. Servs., 157 Fed. Cl. 159, 169 (2021) (finding that a special master

[14] The term "homology" is used when discussing molecular mimicry. "Homology" is defined as "the quality of being homologous; the morphological identity of corresponding parts; structural similarity due to descent from a common form." *Dorland's* at 868.

erred in requiring petitioner submit a study to establish medical theory causally connecting flu vaccine to brachial neuritis).

Here, both Dr. Steinman and Dr. Shoenfeld contribute to Ms. Bravo's claim. The Secretary's experts, Dr. Romberg and Dr. Sriram, oppose this theory. Their opinions regarding molecular mimicry are summarized.

(1) Petitioner's Experts

Dr. Steinman's theory contains several steps. First, Dr. Steinman accesses a resource the National Institute of Health makes available to the public that provides the series of amino acids for numerous proteins, the basic local alignment search tool ("BLAST"). Dr. Steinman enters a protein found in the HPV vaccine, the major capsid L1. Exhibit 70 at 9. Dr. Steinman then enters a protein (myelin basic protein) that, according to Dr. Steinman, is attacked to cause multiple sclerosis. The BLAST program determines the degree to which the sequence of proteins overlap. Dr. Steinman then enters a second protein also potentially involved in the development of multiple sclerosis (myelin oligodendrocyte-glycoprotein) and the BLAST program presents another set of results. (Note: Dr. Sriram disagrees with the assertion that attacks on myelin basic protein and myelin oligodendrocyte-glycoprotein cause multiple sclerosis.) Dr. Steinman next searches the output of sequence similarity to identify places in which five of eleven amino acids are identical. Id. at 10. From this process, Dr. Steinman concluded that the amount of homology between a portion of the HPV vaccine and either myelin basic protein or myelin oligodendrocyte-glycoprotein would allow a person's immune system to misfire. Instead of attacking the vaccine, the immune system attacks host tissue, myelin basic protein or myelin oligodendrocyte-glycoprotein. Id. at 17.

Later, in his fourth report, Dr. Steinman added another step. He consulted a second resource from the National Institute Health, the immune epitope database. Exhibit 349 at 2. The resource shows that the amino acid sequences Dr. Steinman identified in his BLAST searches are found in people. Id. at 8. To Dr. Steinman, this additional step "increased the stringency." Id. at 2.

While Dr. Shoenfeld generally deferred to Dr. Steinman on the topic of molecular mimicry, Dr. Shoenfeld added some different opinions. Dr. Shoenfeld maintained that the adjuvant in the HPV vaccine could enhance an immune-mediated cross-reaction. Exhibit 9 at 11-12.

(2) Respondent's Experts

Both Dr. Romberg and Dr. Sriram disputed the persuasiveness of the theory that an HPV vaccination can worsen multiple sclerosis via molecular mimicry. Dr. Romberg's basic point was that the BLAST searches have produced results with such "a low degree of similarity that [they] cannot be reliably differentiated from a random pairing." Exhibit A at 13. Dr. Romberg's critique rests upon two points. The first is a statistical measurement called an "E value," which is discussed more below. The second is that Dr. Romberg also searched the BLAST program and discovered many proteins in common pathogens that exceeded the degree of homology Dr. Steinman found. Id. at 14.

Dr. Romberg later turned to Dr. Steinman's use of the immune epitope database. Dr. Romberg found Dr. Steinman's results "objectionable" for two reasons. Exhibit H at 4. First, Dr. Steinman "leniently permits epitopes with only 70% homology to his search sequence (the lowest % allowed by the search engine)." Id. Second, Dr. Steinman's technique "filters out all non-immunogenic epitopes which introduces a significant and highly problematic confirmation bias. His searches are designed to hide evidence that an epitope is NOT immunogenic." Id. Dr. Romberg concludes that "this dangerous combination of analytic leniency and susceptibility to confirmation bias does not offer 'filtration' as Dr. Steinman claims but rather contaminates his data with non-random errors that are amplified (not filtered out) as it moves from one analysis tier to the next." Id.

As a neurologist, Dr. Sriram brought a different perspective on Dr. Steinman's molecular mimicry. Dr. Sriram contended that the pathology of multiple sclerosis has not been shown to involve either of the proteins that Dr. Steinman used in his BLAST searches, myelin basic protein and myelin oligodendrocyte-glycoprotein. Exhibit C at 12-13.

(3) Analysis

Introductory Points. A few matters warrant mentioning at the beginning of the analysis. First, Ms. Bravo has advanced this theory in her briefs. E.g. Pet'r's Supp'l Br. at 4. However, Ms. Bravo's arguments are not well developed. For example, after the Secretary challenged many details of the molecular mimicry theory (Resp't's Br. at 24-27), Ms. Bravo's ensuing brief simply repeated much of her prior brief and did not refute the objections the Secretary had interposed. See Pet'r's Reply at 4-5.

Second, special masters have evaluated the theory of molecular mimicry differently. These disparate outcomes may reflect differences among finders of fact. Lampe v. Sec'y of Health & Human Servs., 219 F.3d 1357, 1368 (Fed. Cir. 2000).

Assessment. Ms. Bravo has not met her burden of establishing that molecular mimicry is a persuasive theory to explain how an HPV vaccination can worsen multiple sclerosis. As discussed above, appellate precedents have tended to require petitioners to demonstrate the reliability of the molecular mimicry theory. Considered as a whole, the evidence does not support a finding that Ms. Bravo has crossed that threshold. Specific problems include: (1) the inconsistency with epidemiology, (2) the commonness of short stretches of similarity in amino acids, (3) the failure of Ms. Bravo and Dr. Steinman to establish with preponderant evidence that any similarity is biologically relevant, and (4) the failure of Ms. Bravo and Dr. Steinman to establish with preponderant evidence that any attack on the substance containing the amino acids Dr. Steinman has identified will worsen (or cause) multiple sclerosis.

First, as noted above, large epidemiologic studies, involving hundreds of thousands of people, have not detected an increased incidence of multiple sclerosis among people who received an HPV vaccine. The consistency in the failure to detect any heightened risk led one group of researchers to comment that the "data do not support the interesting hypothesis . . . regarding a biological plausibility based upon a molecular mimicry of the vaccine with myelin basic protein." Mouchet at 114.

Second, overlapping sequences in amino acids are relatively common. Although Dr. Romberg made this point, see Exhibit A at 13, articles that Dr. Shoenfeld cites determined how common homology is. Using one part of the HPV vaccine, a researcher discovered more than eighty sequences in which seven amino acids line up with amino acid sequences in the human genome exactly. Kanduc (Exhibit 321 at 65. Thus, Dr. Steinman's identification of some parts of the HPV vaccine containing some sequences of amino acids that resemble (five out of eleven) some portions of the nervous system is not particularly surprising.

Third, and relatedly, Dr. Steinman has not established that the homologies he identified have any biologic significance. A paper that Dr. Steinman cited in his report (Exhibit 70 at 13) investigated this point. This group of researchers found that bioinformatic "searches for short amino acid sequence matches of eight amino acids or fewer to identify proteins as potential crossreactive allergens is a product

of chance and adds little value to allergy assessments for newly expressed proteins." Silvanovich (Exhibit 84).

Fourth, Dr. Steinman has not established that either myelin basic protein (MBP) or myelin oligodendrocyte-glycoprotein (MOG) is the specific tissue attacked in multiple sclerosis. Dr. Sriram questioned whether "reactivity to either MBP or MOG is sufficient to trigger an autoimmune response." Exhibit C at 13. He added: "In the 50 or [sic] years since autoimmunity to myelin antigens have been suggested as a cause of MS, they have not been proven. Many therapies targeting autoimmune response to MBP antigen have failed." Id. at 12. Although Dr. Steinman responded to Dr. Sriram's report, Dr. Steinman did not address this specific point. See Exhibit 304. Thus, crediting Dr. Steinman's focus on myelin basic protein or myelin oligodendrocyte-glycoprotein is difficult. See Taylor v. Sec'y of Health & Hum. Servs., No. 13-700V, 2018 WL 2050857, at *23 (Fed. Cl. Spec. Mstr. Mar. 9, 2018) (questioning whether Dr. Steinman had presented reliable evidence for the likely target of an attack resulting in acute disseminated encephalomyelitis or multiple sclerosis).

Overall, the gaps and unexplored assumptions in Dr. Steinman's theory that molecular mimicry can worsen (or cause) multiple sclerosis are too much for Ms. Bravo to overcome. She has not presented sufficient evidence to make this theory persuasive. Thus, she has not presented preponderant evidence.

The finding in Ms. Bravo's case is based upon the evidence in her case, although the outcome is consistent with the results in other cases. Maciel v. Sec'y of Health & Hum. Servs., No. 15-362V, 2018 WL 6259230, at *27-28 (Fed. Cl. Spec. Mstr. Oct. 12, 2018); L.Z v. Sec'y of Health & Hum. Servs., No. 14-920V, 2018 WL 5784525, at *17-20 (Fed. Cl. Spec. Mstr. Aug. 24, 2018).

2. Loving Prong 5 / Althen Prong 2

Even if Ms. Bravo had established the persuasiveness and reliability of any theory that the HPV vaccine can worsen (or cause) multiple sclerosis generally, she would still be required to establish with preponderant evidence that the vaccination harmed her specifically. Her proof on this point is also lacking.

As explained in the previous section, among the people whom Ms. Bravo retained, Dr. Steinman is the only one who came close to presenting a persuasive theory of how the HPV vaccine might have injured Ms. Bravo. Thus, his reports are the focus of the next prong as well.

In Dr. Steinman's first report, his section regarding the "Logical Sequence of Cause and Effect" consists of four sentences. Exhibit 70 at 22. These sentences summarize the two potentially causal theories Dr. Steinman put forward. None of these sentences discuss Ms. Bravo at all. Dr. Steinman has not identified any facts in Ms. Bravo's history that support finding the HPV vaccine had any harmful effects.[15]

Dr. Steinman's remaining reports do not meaningfully fill this gap. See Exhibits 133, 304, 359 (addressing MRIs), 400 (addressing opinions of neuroradiologists), 415 (presenting studies on Epstein-Barr virus and multiple sclerosis), 427 (responding to Dr. Romberg's opinion on the Epstein-Barr virus studies).

At best, in the report in which Dr. Steinman explicitly addressed the Loving prongs, his section on "logical sequence" is one sentence. Dr. Steinman states: "The vaccine with significant mimicry with MOG and myelin basic protein triggered an immune response that has been linked to optic neuritis and MS." Exhibit 349 at 13. That is the total of Dr. Steinman's writing on the topic in this report. This content is too conclusory to be persuasive. See Song v. Sec'y of Dep't of Health & Hum. Servs., 31 Fed. Cl. 61, 67–68, (affirming Special Master's decision to give little weight to a doctor's conclusion that the vaccine caused the alleged injuries where the doctor only made conclusory statements without explanation), aff'd, 41 F.3d 1520 (Fed. Cir. 1994); see also Kreizenbeck v. Sec'y of Health & Hum. Servs., No. 08-209V, 2018 WL 3679843, at *32 n.44 (Fed. Cl. June 22, 2018) ("when a petitioner seeks to advance causation theories based on conclusory arguments that . . . reflect conclusory expert statements that are not themselves backed up with reliable scientific support, the absence of such evidence . . . can be noted in evaluating if the petitioner has carried his burden of proof."), mot. for rev. denied, 141 Fed. Cl. 138 (2018), aff'd, 945 F.3d 1362 (Fed. Cir. 2020).

Ms. Bravo's argument matches the thinness of this evidence. She concludes that the HPV vaccine, "when administered to [Ms. Bravo] must have acted upon the [existing] Multiple Sclerosis causing further damage to the area of the brain, resulting in the aggravation of the disease process with the development of serious and disabling clinical signs and symptoms that occurred." Pet'r's Br. at 21.

[15] The sequence of events might be supportive. They are discussed in the following section on timing.

However, Ms. Bravo fails to identify any evidence (other than the sequence of events) to show that a vaccine-induced injury "must have" happened.

The parties were directed to identify any treating doctors who associated Ms. Bravo's neurologic problem with the HPV vaccination. Order, issued March 26, 2021, at 9. Ms. Bravo did not point to any treating doctors helpful to her case. See Pet'r's Br. at 20-21.

In contrast, the Secretary and Dr. Sriram point out that Dr. Langer-Gould treated Ms. Bravo. Resp't's Br. at 29 n.33, citing Exhibit C at 16; see also Exhibit 3 at 446 (identifying Dr. Langer-Gould as a specialist in multiple sclerosis). This relationship is significant to the Secretary because (a) Dr. Langer-Gould has written articles investigating whether vaccines cause multiple sclerosis and (b) did not connect Ms. Bravo's HPV to her multiple sclerosis.

The Secretary could have done more to prove these arguments. The Secretary did not submit any papers by Dr. Langer-Gould, although special masters have discussed such papers. See Harrington v. Sec'y of Health & Hum. Servs., No. 14-43V, 2018 WL 4401976, at *21-22, 24 (Fed. Cl. Spec. Mstr. Aug. 14, 2018).

More significantly, the Secretary has not cited evidence that Dr. Langer-Gould actually knew that Ms. Bravo received the HPV vaccination. See Resp't's Br. at 29. Dr. Langer-Gould's history from her first appointment with Ms. Bravo does not memorialize Ms. Bravo's vaccination. See Exhibit 3 at 404-07. While Dr. Langer-Gould might have constructive knowledge of the vaccination in that it is discussed in the Kaiser medical records, which exceed 1500 pages, ascribing this knowledge to Dr. Langer-Gould seems unjustified.

Ultimately, the Secretary does not bear the burden in this off-Table case to present evidence that treating doctors rejected the claim that the HPV vaccine harmed Ms. Bravo. It is Ms. Bravo's burden to show a "logical sequence of cause and effect" that the HPV vaccine harmed her. The absence of any affirmative statements from treating doctors is one reason she has not met this burden. Quintana v. Sec'y of Health & Hum. Servs., No. 15-1273V, 2022 WL 1873849, at *12, 14 (Fed. Cl. May 18, 2022) (holding that the special master did not convert missing evidence into evidence when she "not[ed] the absence of evidence," as this "is not the same as requiring evidence.").

3. Loving Prong 6 / Althen Prong 3

The next element concerns the timing. At several points, Ms. Bravo emphasizes that her eye problem (optic neuritis) manifested approximately five weeks after her final HPV vaccination. E.g. Pet'r's Br. at 6, 11, 21-22; Pet'r's Supp'l Br. at 2. Her experts also discuss this sequence of events. Exhibit 70 (Dr. Steinman's report in the context of causation-in-fact) at 21; Exhibit 349 (Dr. Steinman's report in the context of significant aggravation) at 13.

Regardless of whether the optic neuritis is treated as the first manifestation of multiple sclerosis for a causation-in-fact case or is treated as a manifestation of an ongoing course of multiple sclerosis for a significant aggravation case, the analysis is the same. Ms. Bravo appears to have credible evidence on this topic. However, proof of a sequence of events in which a vaccination preceded a decline in health does not mean the vaccine caused the problem. Grant v. Sec'y of Health & Human Servs., 956 F.2d 1144, 1148 (Fed. Cir. 1992) ("Temporal association is not sufficient, however, to establish causation in fact."); L.Z v. Sec'y of Health & Hum. Servs., No. 14-920V, 2018 WL 5784525, at *20 ("I cannot conclude from this record that the flu vaccine had anything more than a temporal relationship to Petitioner's MS flare—and such a relationship is well understood in the Program to have little evidentiary bearing when determining entitlement.") (Fed. Cl. Spec. Mstr. Aug. 24, 2018). Thus, her showing on this prong does not overcome her lack of evidence on the other two elements discussed above.

V. A Hearing Is Not Necessary

Special masters possess discretion to decide whether an evidentiary hearing will be held. 42 U.S.C. § 300aa-12(d)(3)(B)(v) (promulgated as Vaccine Rule 8(c) & (d)), which was cited by the Federal Circuit in Kreizenbeck v. Sec'y of Health & Hum. Servs., 945 F.3d 1362, 1365 (Fed. Cir. 2018). "A special master is not obliged to hold an evidentiary hearing." Oliver v. Sec'y of Health & Hum. Servs., 133 Fed. Cl. 341, 354 (2017), aff'd, 900 F.3d 1357, 1363 (Fed. Cir. 2018).

Here, Ms. Bravo has had a fair opportunity to present her case. She presented more than twenty reports from people whom she retained. She argued her position in four briefs regarding her entitlement to compensation. She has not demonstrated how oral testimony would affect the outcome of any of the issues. Accordingly, the undersigned declines to convene a hearing.

VI. Additional Comments

Ms. Bravo and her parents have struggled after the diagnosis of multiple sclerosis. Exhibit 3 at 631-32. The challenges in living with a chronic disease are certainly understandable. They deserve sympathy for their troubles and admiration for how they have tried to address the hardships that have fallen on them.

It is also understandable that Ms. Bravo and her parents might point to the third dose of the HPV vaccination as contributing to her health problems. After all, before the vaccination, no one knew Ms. Bravo had at least one lesion in her brain and no doctor had diagnosed her with multiple sclerosis. Then, from their perspective, Ms. Bravo's health turned upside down after the vaccination. It is easy to blame the vaccination, and the Vaccine Program is the forum that primarily resolves claims that a vaccine injured someone.

Ms. Bravo presented multiple experts and multiple theories in this litigation. The multiplicity has not been advantageous. See Baron v. Sec'y of Health & Human Servs., No. 14-341V, 2019 WL 2273484, at *17 (Fed. Cl. Spec. Mstr. Mar. 18, 2019) (petitioners "need to propose something more than taking a vague 'kitchen sink' approach and listing eleven mechanisms that have been previously submitted in the Program for claims of vaccine-caused injury with various degrees of success. Petitioners have listed many possibilities but have not identified a sound and reliable explanation that can be applied to the vaccines and injury in this case"). As discussed at length above, it appears that Ms. Bravo has disclaimed any reliance upon Dr. Shaw and Dr. Lee by not advancing their opinions with any force in her briefs. Nevertheless, as the Vaccine Act requires, the undersigned has considered this evidence as part of the case.

The undersigned has also evaluated the parts of Ms. Bravo's evidence that are relatively stronger, the reports from Dr. Shoenfeld and Dr. Steinman. While the reports from Dr. Shoenfeld and Dr. Steinman are better than the reports from Dr. Shaw and Dr. Lee, the reports from Dr. Shoenfeld and Dr. Steinman remain unpersuasive for many reasons listed above. Without a persuasive presentation, Ms. Bravo is not entitled to compensation.

VII. Conclusion

Ms. Bravo's case began with an allegation that an HPV vaccination caused her to suffer multiple sclerosis. After the evidence showed, more likely than not, that she had multiple sclerosis before the vaccination, the case transitioned to a claim that the HPV vaccination significantly aggravated the multiple sclerosis.

Regardless of the characterization, the evidence does not preponderate in favor of finding that the HPV vaccination harmed Ms. Bravo. Ms. Bravo has not established with preponderant evidence that the HPV vaccination can worsen (or cause) multiple sclerosis. She also has not established that the HPV vaccination harmed her. Accordingly, Ms. Bravo is not entitled to compensation.

The Clerk's Office is instructed to enter judgment in accordance with this decision unless a motion for review is filed. Information about filing a motion for review, including the deadline, can be found in the Vaccine Rules, available through the Court's website.

IT IS SO ORDERED.

s/Christian J. Moran
Christian J. Moran
Special Master

Appendix: List of Medical Articles Cited[1]

1. R. Inbar et al., Behavioral abnormalities in female mice following administration of aluminum adjuvants and the human papillomavirus (HPV) vaccine Gardasil. 65 IMMUNOLOGIC RES. 136 (2017); filed as Exhibit 346.

2. D. Kanduc, Quantifying the possible cross-reactivity risk of an HPV16 vaccine. 8 J. EXP. THERAPEUTICS & ONCOLOGY 65 (2009); filed as Exhibit 321.

3. D. Kanduc & Y. Shoenfeld, From HBV to HPV: Designing vaccines for extensive and intensive vaccination campaigns worldwide. 15 AUTOIMMUNITY REVIEWS 1054 (2016); filed as Exhibit 322.

4. N.P. Klein et al., Safety of quadrivalent human papillomavirus vaccine administered routinely to females. 166 ARCH. PEDIATR. ADOLESC. MED. 1140 (2012); filed as Exhibit H-2.

5. Lanz et al., Clonally expanded B cells in multiple sclerosis bind EBV EBNA1 and GlialCAM. 603 NATURE 321 (2022); filed as Exhibit 416.

6. Linneberg et al., Association of subcutaneous allergen-specific immunotherapy with incidence of autoimmune disease, ischemic heart disease, and mortality. 129 J. ALLERGY CLIN. IMMUNOL. 413 (2012); filed as Exhibit A-25.

7. J. Mouchet et al., Human papillomavirus vaccine and demyelinating diseases - A systematic review and meta-analysis. 132 PHARMACOL. RES. 108 (2018); filed as Exhibit C-4.

8. National Academies of Sciences, Engineering, and Medicine. Considerations for designing an epidemiologic study for multiple sclerosis and other neurologic disorders in pre and post 9/11 Gulf War veterans. Washington, DC: The National Academies Press; (2015); filed as Exhibit 72.

9. W.H. Robinson & L. Steinman, Epstein-Barr virus and multiple sclerosis. 375 SCIENCE 264 (2022); filed as Exhibit 415.

10. N.M. Scheller et al., Quadrivalent HPV Vaccination and Risk of Multiple Sclerosis and Other Demyelinating Diseases of the Central Nervous System. 313 JAMA 54 (2015); filed as Exhibit A-12.

11. A. Silvanovich et al., The value of short amino acid sequence matches for prediction of protein allergenicity. 90 ToxicolSci 252 (2006); filed as Exhibit 84.

[1] All articles have been considered.

12. I. Sutton et al., CNS demyelination and quadrivalent HPV vaccination. 15 MULT. SCLER. 116 (2009); filed as Exhibit 317.

13. R.L. Ufret-Vincenty et al., In vivo survival of viral antigen-specific T cells that induce experimental autoimmune encephalomyelitis. 188 J. EXP. MED. 1725 (1998); filed as Exhibit 26.

14. C. Zannetti et al. TLR9 transcriptional regulation in response to double-stranded DNA viruses. 193 J. IMMUNOL. BALTIM. MD. 3398 (2014); filed as Exhibit E-1.